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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/402,713	06/13/2000	MARION J. G. BUSSEMAKERS	1619.0020001	6311

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	09/402,713	BUSSEMAKERS, MARION J. G.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 4-10, 12-14, 25-29, 31-33, 35, 37-39, 41-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8-10,27,37,38 and 48-50* is/are allowed.

6)☒ Claim(s) *2,14,39,43-46,53,54 and 57-60* is/are rejected.

7)☒ Claim(s) *4-7,14,25,26,28,29,31-33,35,41,42,47,51,52,55,56 and 112* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/23/2004 has been entered.

Claims 2, 4-10, 12-14, 25-29, 31-33, 35, 37-39, and 41-60 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of rejection.

Inventorship

In view of the papers filed 12/03/2004, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(c). The inventorship of this application has been changed by addition of William B. Isaacs. The application will be processed for correction the inventorship as corrected.

Specification, Withdrawn

The objection of disclosure is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

The rejection of claims 2, 11-26, and 39-45 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in view of the amendment.

The rejection of claims under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is also **withdrawn** in view of the amendment.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 14, 43, 53, and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 14, 43, 53, and 57 are drawn to a non-human organism comprising the recombinant nucleic acids of the base claims that the instant claims depend on.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the

art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification at pages 48-51 discloses that a gene therapy construct using the newly discovered PCA3 gene could be made using an art-known gene therapy vector for use in the "method of treating a PCA3-associated disease (preferably, prostate cancer) in a patient in need of such treatment, a PCA3 P gene which is not indicative of a disease state can be provided to the cells of such patient in a manner and amount that permits the expression of the PCA3 protein provided by such gene, for a time and in a quantity sufficient to treat such patient. Preferably, gene replacement ("knock our') technology is used that would replace the disease causing PCA3 gene with a PCA3 gene which does not cause disease (specifically, prostate cancer)." (Note the paragraph bridging pages 48-49). The specification at pages 57-62 discloses that the newly discovered PCA3 nucleic acid could be used in making transgenic "non-human animals in order to provide animal models for human diseases." (Note page 61, line 17).

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because the amount of guidance, direction, and exemplification set forth therein would not be sufficient to enable the skilled artisan to have a reasonable expectation of success in using the claimed invention without the need to perform additional, and an undue amount of experimentation.

The specification does not provide a sufficient amount of guidance, direction, or exemplification to enable the skilled artisan to make or use the non-human transgenic

animal. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predicable or viable. Houdebine (*Journal of Biotechnology* 1994, 34: 269-287) teaches the vectors to be used for directing the expression of transgenes in any given tissue, or in all tissues, must contain the appropriate regulatory regions. Houdebine teaches expression is heavily dependent on the site of integration in the host genome and the site of integration is presently unpredictable. In addition, Bussenmakers et al., of record (Cancer Res. 1999 Dec 1;59 :5975-90) teach at page 5978, left column, lines 5-7 that the transgenic mice might not be relevant because rodents do not have the corresponding PCA3 gene, i.e. the authors of the publication were not able to detect the corresponding gene under low stringency condition. Therefore, it is concluded that one of skill in the art would need to perform undue experimentation in order to make and use the claimed host comprised within a transgenic animal.

As for the gene therapy, the specification does not teach provide a sufficient amount of guidance, direction, and exemplification to enable the skilled artisan to have a reasonable expectation of a successful gene therapy. The art of gene therapy, i.e., the *in vivo* delivery genetic information to targeted cells within a body using naked DNA or viral vectors or by reintroducing *ex vivo* modified host cells into the body, is still in its infancy. Moreover, the art is highly unpredictable and its successful application has been hindered by numerous limitations, which the specification does not remedy and would preclude the skilled artisan from having a reasonable expectation of successfully

making and using the claimed invention without need of performing an undue amount of experimentation. The art recognizes that gene therapy is not a trivial matter.

The specification does not teach method of gene therapy using the instantly claimed nucleic acid. The specification does not teach any method of overcoming technical difficulties the art has been facing with the gene therapy. For example, Friedmann (Scientific American, June 1997, pages 96-101), Verma and Somia (1997, Nature, vol. 389, pages 239-242), and Rubanyi (2001, Molecular Aspects of Medicine 22, pages 113-142) all teach that gene therapy art still faces major hurdle to overcome. Rubanyi at the abstract teaches that the prerequisite of successful gene therapy includes "therapeutically suitable genes with a proven role in pathophysiology of the disease". The instant specification fails at this first prerequisite because the specification does not teach any therapeutically suitable genes with a proven role in pathophysiology of the disease. Bussenmakers et al., (1999) teach that the instantly claimed nucleic acids might be a non-coding gene. This teaching is at odd with applicant's assertion at the paragraph bridging pages 48 and 49 that the gene therapy "permits the expression of the PCA3 protein provided by such gene" in the non-human organism. In addition, overexpression of the PCA3 transcript is associated with prostate tumor, not under-expression or loss of expression.

Considering the limited guidance, unpredictability in the art, and the broad scope of the claims, it is concluded that undue experimentation is required in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 2, 39, 45-46, 54, and 58-60 are rejected under 35 U.S.C. 102(a) as being anticipated by Bussemakers et al., of record, 87th Annual Meeting of the American Association for Cancer Research, Washington, DC,1996, April 20-24.

The claims are interpreted as drawn to a primer capable of hybridizing to PCA3 , i.e., alias, DD3 according to Bussemakers et al., of record (1999) over-expressed in prostate cancer as compared to human normal tissue selected from the group consisting of artery, brain, breast, duodenum, bladder, colon, heart, liver, lung, ovary, pancreas, placenta, seminal vesicles, skeletal muscle, skin, spinal cord, spleen and testis, or as compared to cancer cell lines selected from the group consisting of: ALVA-3I, DU145, JCA-I, PPC-I, PC3, and TSU-Pr1 under the specified conditions of base claims 2, and 46, and 54, wherein the length of said primer is 10-50 nucleotides.

Bussemakers et al., in 3rd paragraph, line 4 teach "DD3-specific primers", and also teach that the primers are used to detect the DD3 human gene products that are over-expressed in prostate cancer as compared to human normal tissue selected from the group consisting of artery, brain, breast, duodenum, bladder, colon, heart, liver, lung, ovary, pancreas, placenta, seminal vesicles, skeletal muscle, skin, spinal cord,

spleen and testis, or as compared to cancer cell lines selected from the group consisting of: ALVA-3I, DU145, JCA-I, PPC-I, PC3, and TSU.

Applicant at pages 8 and 9 of the Remark section of the amendment filed on 07/15/2002 argued that Bussemakers et al., do not teach any sequence nor do they characterize the genomic structure of DD3. Bussemakers et al., do not teach an open reading frame of DD3, complexity of the genome organization due to an alternative splicing, as well as other uncertainty as to the nature of the DD3.

These arguments have been fully considered but found unpersuasive because applicant's arguments are not commensurate in scope of the claims. The Markush species of (e) in each of the base claims 2, 46, and 54 are not limited to the nucleic acid sequence of a DD3 gene. The claims as currently construed read on "DD3-specific primers".

The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the "DD3-specific primers" of the prior art does not possess the same material, structural characteristics of the instantly claimed nucleic acid. The DD3-specific primers of the prior art possess the same functional characteristics as the instantly claimed primer sequences, i.e. detecting mRNA over-expressed prostate cancer as compared to human normal tissue selected from the group consisting of artery, brain, breast, duodenum, bladder, colon, heart, liver, lung, ovary, pancreas, placenta, seminal vesicles, skeletal muscle, skin, spinal cord, spleen and testis, or as compared to cancer cell lines selected from the group consisting of: ALVA-3I, DU145, JCA-I, PPC-I, PC3, and TSU. In the absence of evidence to the

contrary, the burden is on the applicant to prove that the claimed primer is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Allowable Subject Matter

Claims 8-10, 27, 37, 38, 48-50 allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Judy Ladringan for Art Unit 1642 whose telephone number is 571-272-0536.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
3/10/05